UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

DATE: March 26, 2019

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

SUBJECT: Risk Assessment for FIFRA Section 3 Registration of the Plant Growth Regulator, 1,4-dimethylnaphthalene (1,4-DMN) (TGAI) and End Use Product DMN EUP containing 97.64% 1,4- dimethylnaphthalene.

Decision Number:	540336, 540337
DP Number:	447035, 447038
Submission Number:	1018183, 1018185
EPA File Symbol Number:	2749-LIL, 2749-LIA
Active Ingredient Type:	Biochemical
PC Code:	055802
CAS Number:	571-58-4
Active Ingredient Tolerance/Exemption:	40 CFR §180.1142
MRID Numbers:	43082507 - 43082518; 43266803; 43594501
PRIA Code:	B672

FROM: Judy Facey, Ph.D., Toxicologist
Risk Assessment Branch
Biopesticides & Pollution Prevention Division (7511P)

JUDY FACEY Digitally signed by JUDY FACEY Date: 2019.03.26 10:04:51 -04'00'

THROUGH: Cathy Eiden, Senior Advisor
Risk Assessment Branch
Biopesticides & Pollution Prevention Division (7511P)

Eiden, Catherine Digitally signed by Eiden, Catherine Date: 2019.03.26 11:00:55 -04'00'

TO: Menyon Adams, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

On behalf of Aceto Agricultural Chemicals Corporation, Product and Regulatory Associates, LLC, has applied for the registration of a new unregistered source of the technical grade active ingredient 1,4-dimethylnaphthalene (1,4-DMN) 97.64% (EPA File Symbol: 2749-LIL) and an end-use product (EP) DMN EUP (EPA File Symbol: 2749-LIA). In support of the registration, the applicant submitted proposed labels, Confidential Statements of Formula (CSF) dated 03-30-2018, a data matrix dated 04-03-2018, and product chemistry and human health assessment data information.

EXECUTIVE SUMMARY

1,4- dimethylnaphthalene technical is intended for formulation into a plant growth regulator for use on post-harvest potatoes during storage or for use on seed potatoes. BPPD has reviewed and evaluated the submitted data for the registration of the unregistered source of 1,4- dimethylnaphthalene, DMN TECHNICAL (EPA File Symbol: 2749-LIL) and the end use product, DMN EUP (EPA File Symbol: 2749-LIA). All data requirements have been met.

BACKGROUND

Biopesticide Use Pattern

Aceto Agricultural Chemicals Corporation is registering the biochemical technical grade active ingredient (TGAI) product DMN TECHNICAL, which is substantially similar to the EPA registered TGAI product 1,4Sight® Technical (EPA Reg. No. 67727-2), containing the active ingredient 1,4 dimethylnaphthalene. The TGAI is intended for use in the formulation into a plant growth regulator for use on post-harvest potatoes during storage or use on seed potatoes. The end-use product (DMN EUP) is a plant growth regulator used as an aerosol fog to enhance the dormancy of [seed] potatoes [(and other root and tuber crops, bulb crops, and ornamental flowering bulbs)] [prior to germination] [or] [during storage phase]. Personal Protective Equipment (PPE) requirements are listed on the label; there are no residential uses. The product is applied at a rate of 1 lb of active ingredient per 50,000 lbs (500 cwt). All proposed uses are indoor and /or contained, thus eliminating the potential for exposure to terrestrial and aquatic environments.

1. STUDY SUMMARIES

Confidential Statement of Formula (CSF)

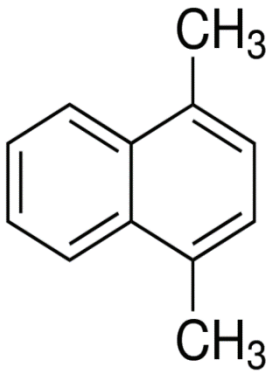
The nominal concentrations and certified limits are listed in Table 1 (see CONFIDENTIAL APPENDIX) for the ingredients in DMN TECHNICAL (EPA File Symbol: 2749-LIL).

Active Ingredient Characterization

The active ingredient (1,4- DMN) is a plant growth regulator which works via suppression of sprout formation and is applied to potatoes during storage and shipping. 1,4- DMN provides short-term suppression of sprouting. 1,4- DMN is a plant growth regulator belonging to the chemical family of alkyl-substituted naphthalenes. This compound is a naturally occurring plant biochemical in potatoes at high enough concentrations to prevent sprouting; however, under suitable conditions there is a decrease of the chemical in potatoes and spouting occurs (1,4 Dimethylnaphthalene Fact Sheet, 2001). The manufacturing process for 1,4-DMN TECHNICAL is a one-step batch process. The final 1,4- DMN TECHNICAL product is verified by analysis. All product chemistry data requirements have been satisfied for the sources of the active ingredients. The applicant cited acceptable MRIDs on the data matrix for all requirements.

Physical and Chemical Characteristics

Technical Name: Naphthalene, 1,4-dimethyl-
Common Name: 1,4-Dimethylnaphthalene (1,4- DMN)
Molecular Formula: $C_{12}H_{12}$
Molecular Weight: 156.33



Chemical Structure of 1,4-Dimethylnaphthalene (1,4-DMN): MRID 50565401

A. Product Chemistry (Technical Product and End-Use Product)

Apart from the storage stability and corrosion characteristics data requirements (studies not submitted), all product chemistry data requirements have been satisfied for the proposed TGAI product and End-use product. The applicant cited acceptable MRIDs on the data matrix for all requirements. Refer to Tables 1 and 2 below for a summary of the product chemistry data (Table 1) and physical and chemical characteristics data (Table 2) submitted to support the product chemistry data requirements.

Table 1. Product Chemistry Data Requirements for DMN TECHNICAL (EPA File Symbol#: 2749-LIL)

OCSPP Guideline Reference No./Study	Description of Result	MRID
880.1100. Product identity and composition	The product identity and composition were adequately addressed.	50565401
880.1200. Description of starting materials, production, and formulation process	The description of the starting materials, production, and formulation process were adequately addressed.	50565401
880.1400. Discussion of formation of impurities	The discussion of formation of impurities was adequately addressed.	50565401
830.1700. Preliminary analysis	The preliminary analysis had been adequately addressed.	50565401
830. 1750. Certified limits	The certified limits listed on the CSF are acceptable.	50565401

TABLE 2. Physical and Chemical Properties of DMN TECHNICAL (40 CFR § 158.2030)			
OCSPP Guideline	**Property**	**Description of Result**	**MRID**
830.6302	Color	Slight tine/ pale yellow	50565403
830.6303	Physical State	Clear liquid	50565403
830.6304	Odor	Petroleum-like	50565403
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Stable at normal temp.; 6-7% loss at elevated temp.; stable in the presence of metals.	43082509
830.6315	Flammability	>100 °C	50565403
830.6317	Storage Stability	**Required data. Not submitted.**	
830.6319	Miscibility	Product is not to be diluted in petroleum solvents, so this data requirement is not triggered.	50565405
830.6320	Corrosion Characteristics	**Required data. Not submitted.**	
830.7000	pH	This study is not required based on the proposed use pattern. 1,4- DMN Technical is a liquid technical and not designed to be dispersed in water	50565405
830.7050	UV/Visible Light Absorption	230-232 nm	50565404
830.7100	Viscosity	Centistokes: 4.5@ 20 °C and 2.6@ 40 °C	50565403
830.7200	Melting Point/Range	Product is a liquid, so this data requirement is not triggered.	50565405
830.7220	Boiling Point/Range	264.9 °C	50565404
830.7300	Density	1.015 g/mL @ 22 °C	50565403
830.7520	Particle Size, Fiber Length and Diameter Distribution	This product is soluble in water, so this data requirement is not triggered.	50565405
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Product is soluble in water, so this data requirement is not triggered.	50565405
830.7840	Water Solubility	5.1 ppm @ 25 °C	43082507
830.7950	Vapor Pressure	2.5 Pa @ 25 °C; 1.88 x 10-2 Torr @ 25 °C 4.85Pa @ 35 °C 11.7 Pa @ 45 °C	43082508

I. Human Health Assessment

A. Active Ingredient

All human health assessment data requirements have been satisfied and a new risk assessment for 1,4-dimethylnaphthalene (1,4-DMN) is not required at this time. The applicant cited acceptable MRIDs in the data matrix to satisfy the data requirements. BPPD's current risk assessments are sufficient to evaluate the use of this active ingredient in the proposed product because the use pattern of this product is similar to that of currently registered product 1,4Sight® Technical (EPA Reg. No. 67727-2). All proposed uses are indoor and /or contained, thus eliminating the potential for exposure to terrestrial and aquatic environments. Minimal exposure is anticipated, and the chemical degrades rapidly into non-toxic components. PPEs are included on the label that will further reduced exposure to workers. In addition, an exemption from the requirement of a tolerance is established for residues of the plant growth regulator, 1,4- dimethylnaphthalene (1,4- DMN), when

applied postharvest to all sprouting root, tuber, and bulb crops in accordance with good agricultural practices (40 CFR § 180.1142).

B. End-Use Product

Acute toxicity data (acute oral, acute dermal, acute inhalation, primary eye, primary dermal and skin sensitization) are required for EPs (DMN EUP). To satisfy these data requirements, the applicant requested to use the toxicity information from the submitted information on the TGAI DMN TECHNICAL.

C. Toxicology

1. Acute and Subchronic Toxicity

All human health assessment data requirements have been satisfied for the proposed TGAI product DMN TECHNICAL (EPA File Symbol: 2749-LIL), containing 97.64% 1.4-dimethylnaphthalene and DMN EUP (EPA File Symbol: 2749-LIA). Refer to Table 3 below for a summary of the data submitted for the acute and subchronic toxicity studies.

Table 3 Mammalian Toxicology Data Requirements for DMN TECHNICAL and DMN EUP (40 CFR § 158.2050)			
Study/OCSPP Guideline No.	**Results**	**Toxicity Category**	**MRID**
Acute oral toxicity (rat) (870.1100)	LD_{50} = 2730 (95 % C.L. 2346- 3178) mg/kg (males and females using the Up-and Down Method) Acceptable/ Guideline	III	43082510
Acute dermal toxicity (rabbit) (870.1200)	LD_{50} > 2,000 mg/kg bodyweight Acceptable/ Guideline	III	43082511
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 4.16 mg/L (4-hr nose-only exposure) Acceptable/ Guideline	IV	43082512
Primary eye irritation (rabbit) (870.2400)	Moderately irritating. Moderate ocular irritation was observed in all rabbits at 24 hours post-treatment with clearance by day 21. Acceptable/ Guideline	II	43082513
Primary dermal irritation (rabbit) (870.2500)	Slight irritation. After treatment, very slight to slight erythema was observed in all males and females through 72 hours with persistence in females until day 7. Well-defined to moderate edema was observed in all males and females within 24 hours post-treatment. At 71 hours, slight edema was observed in one male and one female. Acceptable/ Guideline	IV[1]	43082514
Dermal sensitization (mouse) (870.2600)	Not a dermal sensitizer. Acceptable/ Guideline	--	43082515
90-Day oral toxicity (rat) (870.3100)	Waived. 1,4-DMN rapidly degrades into non-toxic components and have been granted an exemption from the need for a tolerance. Potatoes ingested by consumers are not sprouting and contain 1,4-DMN. The aerosol fog application will not increase 1,4- DMN levels above those found in a potato when typically consumed.	--	50565406
90-Day dermal toxicity (rat) (870.3250)	Waived. Prolonged dermal exposure is not expected based on the use pattern and appropriate PPE requirements and re-entry restrictions on label of end-use product. Product is applied as aerosol in indoor potato storage facilities and applicators/ handlers must vacate premises during treatment.	--	50565406
90-Day inhalation toxicity (rat) (870.3465)	Waived. Significant repeated inhalation exposure is not expected based on the use pattern of aerosol fog application to potatoes in storage. Premises are ventilated prior to re-entry and handlers must wear respirators.	--	50565406

Table 3 Mammalian Toxicology Data Requirements for DMN TECHNICAL and DMN EUP (40 CFR § 158.2050)			
Study/OCSPP Guideline No.	**Results**	**Toxicity Category**	**MRID**
Developmental toxicity (870.3700)	Waived. 1,4-DMN rapidly degrades into non-toxic components and have been granted an exemption from the need for a tolerance. Potatoes ingested by consumers are not sprouting and contain 1,4-DMN. The aerosol fog application will not increase 1,4-DMN levels above those found in a potato when typically consumed.	--	50565406
Mutagenicity (Bacterial reverse Mutation) (870.5100)	Not mutagenic under the conditions of the study. Mutagenicity was not observed with or without metabolic activation in any of the 5 strain of *Salmonella typhimurium* tested.	--	43082516
In vitro Mutagenicity (Unscheduled DNA synthesis in mammalian cells) (870.5550)	Not genotoxic under the conditions of the study. No induction of nuclear grain counts in hepatocytes was observed at the tested concentration range of 0.25 µg/mL to 10 µg/mL	--	43082517
In vivo Mutagenicity (Mammalian erythrocyte micronucleus test) (870.5395)	Not mutagenic under the conditions of the study. There was no increase in the number of micronuclei per 1,000 polychromatic erythrocytes in the bone marrow of mice at doses of 225 mg/kg, 450 mg/kg and 900 mg/kg 1,4-DMN. A decrease in the polychromatic erythrocyte (PCE) and normochromatic erythrocyte (NCE) ratio was observed with increased doses of the chemical.	--	43082518

[1]Originally classified as Toxicity Category III; however, the results of the study and the information provided under 40 CFR §156.62 indicate that the chemical should be classified into Toxicity Category IV.

RECOMMENDATIONS AND CONCLUSIONS

1. Storage stability and corrosion characteristics studies were not submitted. These are required product chemistry data and must be submitted to the Agency. All other product chemistry data submitted for this registration application are ACCEPTABLE.

2. The submitted basic CSFs for DMN TECHNICAL (EPA File Symbol: 2749-LIL) dated 03-30-2018 and DMN EUP (EPA File Symbol: 2749-LIA) are ACCEPTABLE.

3. The cited studies in support of this registration application for the acute and subchronic toxicity studies are ACCEPTABLE. DMN TECHNICAL (EPA File Symbol: 2749-LIL) and DMN EUP (EPA File Symbol: 2749-LIA) can be classified as Category II for primary eye irritation, Category III for acute oral and acute dermal toxicity, and Category IV for acute inhalation and primary dermal irritation. The product is not a skin (dermal) sensitizer.

BIBLIOGRAPHY OF STUDIES

MRID 43082507 through 43082518: ACCEPTABLE
MRID 43266803 ACCEPTABLE
MRID 43594501 ACCEPTABLE

U.S. EPA. Memorandum from Angela Gonzales to Leonard Cole. Toxicology Scoping Document for the Registration Review of 1,4-Dimehtylnaphthalene and 2,6-Diisopropylnaphthalene. U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. August 20, 2012.

U.S. EPA. Memorandum from Gina Burnett to Colin Walsh. Product Chemistry Scoping Document for the Registration Review of 1,4-Dimehtylnaphthalene (1,4- DMN) and 2,6-Diisopropylnaphthalene (2,6- DIPN). U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. August 22, 2012.

U.S. EPA. Memorandum from Angela Gonzales to Leonard Cole. Toxicology Scoping Document for the Registration Review of 1,4-Dimehtylnaphthalene and 2,6-Diisopropylnaphthalene. U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. February 20, 2013.

U.S. EPA. 1,4- Dimethylnaphthalene (055802) Fact Sheet. U.S. Environmental Protection Agency, Office of Pesticide Programs.

cc: J. Facey, Ph.D., C. Eiden, M. Adams, BPPD Science Review File, Documentum
J. Facey, Ph.D., Toxicologist, FT, PY-S: March 26, 2019.

CONFIDENTIAL APPENDIX

TABLE 1. Basic Nominal CSF concentrations and certified limits for DMN TECHNICAL (EPA File Symbol: 2749-LIL)[a].

Ingredients (CAS number)	PC Code	Purpose	Concentration (% by weight)		
			Nominal	Upper	Lower
Active Ingredient					
1,4- dimethylnaphthalene CAS No. 571-58-4		Active Ingredient EPA Reg. #:	97.64	99.9	94.71
[redacted]					

Data taken from the CSF dated 03-30-2018 and MRID 50565401.

Inert ingredient information may be entitled to confidential treatment

Description of Production Starting Materials

[redacted]

Discussion of Formation of Impurities

[redacted]

Manufacturing process information may be entitled to confidential treatment

Quality control process information may be entitled to confidential treatment